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NONLINEAR CONFORMATION OF SECONDARY PROTEIN FOLDING

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A model to describe the mechanism of conformational dynamics in secondary protein based on matter interactions is proposed. The approach deploys the lagrangian method by imposing certain symmetry breaking. The protein backbone is initially assumed to be nonlinear and represented by the Sine-Gordon equation, while the nonlinear external bosonic sources is represented by ϕ^4 interaction. It is argued that the nonlinear source induces the folding pathway in a different way than the previous work with initially linear backbone. Also, the nonlinearity of protein backbone decreases the folding speed.

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1. Introduction

It is known that the nonlinear excitations play an important role conformational dynamics. For instance, the effective bending rigidity of a biopolymer chain could lead to a buckling instability [1]. Some models have then been proposed to explain such protein transition [2,3,4,5,6,7,8,9].

In our previous work, the conformational dynamics of secondary protein can be modeled using ϕ^4 interactions [10,11]. It has been shown that the model has reproduced the toy ad-hoc model based on the set of nonlinear Schrödinger (NLS) and nonlinear Klein-Gordon equation of motions (EOMs) in a more natural way

from first principle [6]. In the model, the unfolding state of protein is initially assumed to be linear. On the other hand, the folding pathway is induced by the nonlinear sources like laser. Both protein conformation changes and the injected non-linear sources are represented by the bosonic lagrangian with an additional ϕ^4 interaction for the sources. It has been argued that the 'tension force' which enables the folded pathway can be reproduced naturally in the EOM.

In this paper, we consider the nonlinear unfolding protein at the initial state, while the external sources remain nonlinear as previously done. This is important to investigate whether the folding mechanism and speed are influenced by the initial conformational state. Otherwise one cannot determine if the folded pathways are really induced and dominated by the nonlinear sources or not.

The paper is organized as follows. First the model under consideration is presented briefly, followed by the numerical analysis of the EOM induced by the model. Finally it is summarized by short discussion of the results and subsequent conclusion.

2. The model

This work is an extension of the previous model on protein folding using lagrangian approach [10,11]. In contrast with the previous model which assumes the initial conformational state is linear, now the protein is initially assumed to be nonlinear likes Sine-Gordon soliton,

$$\mathcal{L}_c = \frac{1}{2}\left(\partial_\mu\phi\right)^\dagger\left(\partial^\mu\phi\right) + \frac{m_\phi^4}{\lambda_\phi}\left[1-\cos\left(\frac{\sqrt{\lambda_\phi}}{m_\phi}|\phi|\right)\right] . \tag{1}$$

However, the sources injected into the backbone remain nonlinear and massless. Then, same as before the nonlinear sources are modeled by ψ^4 self-interaction.

$$\mathcal{L}_s = \frac{1}{2}\left(\partial_\mu\psi\right)^\dagger\left(\partial^\mu\psi\right) + \frac{\lambda_\psi}{4!}\left(\psi^\dagger\psi\right)^2 . \tag{2}$$

The interaction term between both is described by,

$$\mathcal{L}_{int} = -\Lambda\left(\phi^\dagger\phi\right)\left(\psi^\dagger\psi\right) . \tag{3}$$

All of them provide the underlying model in the paper with total potential,

$$V_{\rm tot}(\psi,\phi) = \frac{m_\phi^4}{\lambda_\phi}\left[1-\cos\left(\frac{\sqrt{\lambda_\phi}}{m_\phi}|\phi|\right)\right] + \frac{\lambda_\psi}{4!}\left(\psi^\dagger\psi\right)^2 - \Lambda\left(\phi^\dagger\phi\right)\left(\psi^\dagger\psi\right) . \tag{4}$$

Now, throughout the paper let us assume that λ_ϕ is small enough, that is approximately at the same order with λ_ψ. In this case, the first term can be expanded in term of $\sqrt{\lambda_\psi}$,

$$V_{\rm tot}(\psi,\phi) \approx \frac{m_\phi^2}{2}\,\phi^\dagger\phi - \frac{\lambda_\phi}{4!}\left(\phi^\dagger\phi\right)^2 + \frac{\lambda_\psi}{4!}\left(\psi^\dagger\psi\right)^2 - \Lambda\left(\phi^\dagger\phi\right)\left(\psi^\dagger\psi\right) . \tag{5}$$

up to the second order accuracy. If $\lambda_\phi = 0$, the result coincides to the case in the earlier work [10]. Imposing namely local U(1) symmetry breaking to the total lagrangian makes the vacuum expectation value (VEV) of the fields yields the non-trivial solutions. In the preceding model, the 'tension force' which plays an important role to enable folded pathway has appeared naturally by concerning the minima of total potential in term of source field [10].

$$\langle\psi\rangle = \sqrt{\frac{12\Lambda}{\lambda_\psi}}\langle\phi\rangle \ . \tag{6}$$

Beside of that, in term of conformation changes field the VEV is,

$$\langle\phi\rangle = \sqrt{\frac{6m_\phi^2 - 12\Lambda\langle\psi\rangle^2}{\lambda_\phi}} \ . \tag{7}$$

It shows that the existence of Sine-Gordon potential makes the early stable ground state of conformational field turns out to be metastable. In other words, the non trivial VEV in Eq. (7) constitutes new more stable ground state of the conformational field. Transition between metastable into stable state breaks the symmetry of the vacuum spontaneously, while the conformational field should be nonlinear even though the external nonlinear source has not been instilled. Therefore the protein backbone should be in nonlinear form at the initial stage.

The symmetry breaking at the same time shifts the mass term of ϕ as follow,

$$m_\phi^2 \to \overline{m}_\phi^2 \equiv m_\phi^2 - \frac{24\Lambda^2}{\lambda_\psi}\langle\phi\rangle^2 \ . \tag{8}$$

Nevertheless, the nonlinear source field is set being massless, since it represents a bunch of light source like laser. Thus, the broken symmetry of conformational field should not be considered to introduce its mass.

3. The EOMs

Having the total lagrangian at hand, one can derive the EOM using the Euler-Lagrange equations,

$$\frac{\partial\mathcal{L}_{\rm tot}}{\partial|\phi|} - \partial_\mu\frac{\partial\mathcal{L}_{\rm tot}}{\partial(|\partial_\mu\phi|)} = 0 \quad \text{and} \quad \frac{\partial\mathcal{L}_{\rm tot}}{\partial|\psi|} - \partial_\mu\frac{\partial\mathcal{L}_{\rm tot}}{\partial(|\partial_\mu\psi|)} = 0 \ , \tag{9}$$

where $\mathcal{L}_{\rm tot} = \mathcal{L}_c + \mathcal{L}_s + \mathcal{L}_{\rm int}$ in Eqs. (1), (2) and (3) respectively.

Substituting Eqs. (1), (2) and (3) into Eq. (9), one immediately obtains a set of EOMs,

$$\frac{\partial^2|\phi|}{\partial x^2} - \frac{1}{c^2}\frac{\partial^2|\phi|}{\partial t^2} + 2\Lambda\,|\phi||\psi|^2 - \frac{m_\phi^3c^3}{\hbar^3\sqrt{\lambda_\phi}}\,\sin\left(\frac{\sqrt{\lambda_\phi}}{m_\phi}|\phi|\right) = 0 \ , \tag{10}$$

$$\frac{\partial^2|\psi|}{\partial x^2} - \frac{1}{c^2}\frac{\partial^2|\psi|}{\partial t^2} + 2\Lambda\,|\psi||\phi|^2 - \frac{\lambda_\psi}{6}\,|\psi|^3 = 0 \ . \tag{11}$$

Here the natural unit is restored to make the light velocity c and $\hbar$ reappear in the equations. The last terms in Eqs. (10) and (11) determine the non-linearity of backbone and source respectively. Also, the protein mass term is melted in the Sine-Gordon potential. One should put an attention in the second last term of Eq. (10), *i.e.* $\sim k\,\phi$ with $k \sim 2\Lambda\langle\psi\rangle^2$. This actually induces the tension force which is responsible for the dynamics of conformational field and enabling the folded pathway as expected.

Hence, solving both EOMs in Eqs. (10) and (11) simultaneously would provide the contour of conformational changes in term of time and one-dimensional space components. The EOMs will be solved numerically using forward finite difference method as done in the previous work [10,12].

4. Numerical solution of EOMs

Same as before, it is more convenient to replace ψ and ϕ with u and w respectively and rewritten it in explicit discrete forms as follows,

$$u_{i,j+1} = 2u_{i,j} - u_{i,j-1} + c^2\epsilon^2 \left(\frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\delta^2} + 2\Lambda w_{i,j}^2 u_{i,j} - \frac{\lambda_\psi}{6} u_{i,j}^3 \right) , \tag{12}$$

$$w_{i,j+1} = 2w_{i,j} - w_{i,j-1} + c^2\epsilon^2 \left(\frac{w_{i+1,j} - 2w_{i,j} + w_{i-1,j}}{\delta^2} + 2\Lambda u_{i,j}^2 w_{i,j} - \frac{m_\phi^3 c^3}{\hbar^3\sqrt{\lambda_\phi}} \sin\left(\frac{\sqrt{\lambda_\phi}}{m_\phi} w_{i,j} \right) \right) , \tag{13}$$

for $i = 2, 3, \cdots, N-1$ and $j = 2, 3, \cdots, M-1$. Forward iterative procedure of the discrete EOMs can be performed if the two lowest time values are known. First, the value at t_1 is fixed by the following boundary conditions,

$$\begin{aligned} &\psi(0,t) = \psi(L,t) = 0 \ \text{ and } \ \phi(0,t) = \phi(L,t) = 0 && \text{for } 0 \le t \le b\ , \\ &\psi(x,0) = f(x) \ \text{ and } \ \phi(x,0) = p(x) && \text{for } 0 \le x \le L\ , \\ &\frac{\partial\psi(x,0)}{\partial t} = g(x) \ \text{ and } \ \frac{\partial\phi(x,0)}{\partial t} = q(x) && \text{for } 0 < x < L\ , \end{aligned} \tag{14}$$

with $f(x)$, $p(x)$, $g(x)$ and $q(x)$ are newly introduced auxiliary functions. Secondly, the values at t_2 can be determined using second order Taylor expansion,

$$u_{i,2} = f_i - \epsilon g_i + \frac{c^2\epsilon^2}{2} \left(\frac{f_{i+1} - 2f_i + f_{i-1}}{\delta^2} + 2\Lambda p_i^2 f_i - \frac{\lambda_\psi}{6} f_i^3 \right) , \tag{15}$$

$$w_{i,2} = p_i - \epsilon q_i + \frac{c^2\epsilon^2}{2} \left(\frac{p_{i+1} - 2p_i + p_{i-1}}{\delta^2} + 2\Lambda f_i^2 p_i - \frac{m_\phi^3 c^3}{\hbar^3\sqrt{\lambda_\phi}} \sin\left(\frac{\sqrt{\lambda_\phi}}{m_\phi} p_i \right) \right) , \tag{16}$$

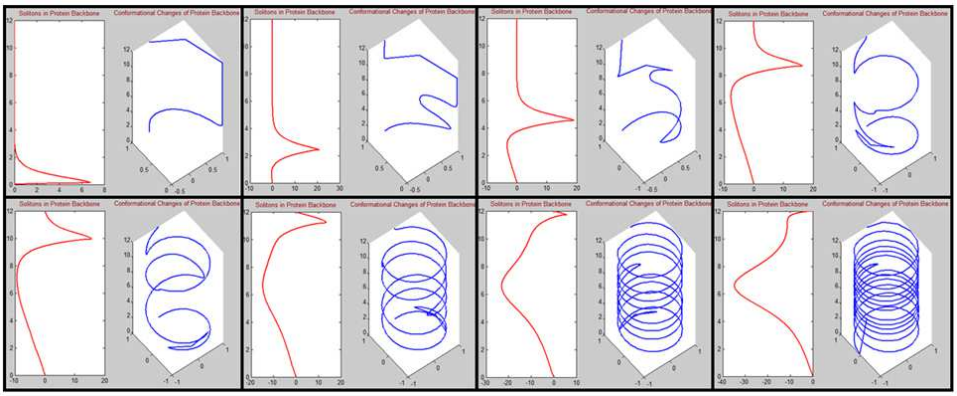

Fig. 1. The soliton propagations and conformational changes on the protein backbone inducing protein folding. The vertical axis in soliton evolution denotes time in second, while the horizontal axis denotes its amplitude. The conformational changes are on the (x, y, z) plane. The constants of the simulation are chosen as $m = 0.08\ eV \equiv 1.42 \times 10^{-37}\ kg, L = 12\ eV^{-1} \equiv 2,364\ nm, \Lambda = 2.83 \times 10^{-3}, \lambda_\psi = 5 \times 10^{-3}, \lambda_\phi = 6 \times 10^{-3}$, and $\hbar = c = 1$.

for $i = 2, 3, \cdots, N-1$. $\delta = \Delta x$ and $\epsilon = \Delta t$ constitutes the side length between the discretized value.

At the initial stage, suppose the nonlinear source and conformation fields have particular form of $f(x) = 2\text{sech}(2x)\, e^{i2x}$ and $g(x) = \arctan[\exp(4x - 10)]$, while $g(x) = q(x) = 0$ for the sake of simplicity. Furthermore, the numerical solutions can be obtained by iterative procedure against Eqs. (12) and (13) using the results in Eqs. (15) and (16) with the boundary conditions in Eq. (14).

The procedure has been performed numerically and the results are given in Fig. 1. The left figures in each box describe the propagation of nonlinear sources in protein backbone, while the right ones show how the protein is folded according to the time evolution. From the figure, it is clear that the protein backbone is infinitesimally bending at the initial stage before the nonlinear source injection. The bending constitutes the contribution of Sine-Gordon potential into the conformation field. However, this bending is too small to generate folding pathway, then the backbone still remains unfolded.

The conformation changes which generate the folding pathway start appearing as the soliton starts propagating over the backbone. The result is surprisingly, even slightly, different with the earlier work. The folding processes are slower than the linear conformation case [10]. It might be considered as an effect of the nonlinear conformational field. One may conclude here that the effect is destructive against the nonlinearity of nonlinear sources. It can also be recognized from Eq. (5) that the nonlinear terms of both fields have opposite sign.

It should be remarked that the results are obtained up to the second order

accuracy in Taylor expansion. In order to guarantee that the numerical solutions contain no large amount of truncation errors, the step sizes δ and ϵ are kept small enough. Nevertheless, the present method should still be good approximation to describe visually the mechanism of secondary protein folding.

5. Conclusion

An extension of phenomenological model describing the conformational dynamics of secondary proteins is proposed. The model is based on the matter interactions among relevant constituents, namely the nonlinear conformational field and the nonlinear sources. The fields are represented as the bosonic fields ϕ and ψ in the lagrangian. It has been shown that from the bosonic lagrangian with ψ^4 self-interaction, the nonlinear and tension force terms appear naturally as expected, and coincide with some previous works [6,10].

However the present model has different contour, and the folding process is getting slower since the EOMs governing the whole dynamics are the nonlinear Sine-Gordon and nonlinear Klein-Gordon equations. It is argued that the nonlinearity of the both fields are against each other. Note that the model is a generalization of earlier models which deployed both linear, or the linear and nonlinear equations.

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References

1. S. F. Mingaleev, Y. B. Gaididei, P. L. Christiansen and Y. Kivshar, *Europhys. Lett.* **59**, p. 403 (2002).
2. S. Caspi and E. Ben-Jacob, *Europhys. Lett.* **47**, p. 522 (1999).
3. S. Caspi and E. Ben-Jacob, *Phys. Lett. A* **272**, p. 124 (2000).
4. A. G. Garcia and J. N. Onuchi, *Proc. Natl. Acad. Sci. USA* **100**, p. 13898 (2003).
5. J. N. Onuchi and P. G. Wolynes, *Curr. Opin. Struct. Biol.* **14**, p. 70 (2004).
6. N. G. Berloff, *Phys. Lett. A* **337**, p. 391 (2005).
7. A. Sulaiman and L. T. Handoko, *J. Comp. Theor. Nanosci.* **8**, 124 (2011).
8. A. Sulaiman, F. P. Zen, H. Alatas and L. T. Handoko, *Phys. Rev. E* **81**, p. 061907 (2010).
9. A. Sulaiman, F. P. Zen, H. Alatas and L. T. Handoko, Statistical mechanics of davydov-scott's protein model in thermal bath, in *Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity*, *Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity* 2011.
10. M. Januar, A. Sulaiman and L. T. Handoko, *Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity* , 472 (2011).

11. M. Januar, A. Sulaiman and L. T. Handoko, The statistical properties of protein folding in the ϕ^4 theory arXiv:1112.4712, (2011).
12. J. H. Mathews and K. D. Fink, *Numerical Methods using Matlab 4th Ed.* (Prentice-Hall, 2004).